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EXAMINER	
MARVICH, MARIA	
ART UNIT	**PAPER NUMBER**
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/763,479	MITTAL ET AL.	
	Examiner	Art Unit	
	Maria B. Marvich, PhD	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,15-34,37,43-47,50-54,56-58,60,61,63-77 and 97-102* is/are pending in the application.

4a) Of the above claim(s) *7 and 75-77* is/are withdrawn from consideration.

5)☒ Claim(s) *6* is/are allowed.

6)☒ Claim(s) *1-4,8-12,15-22, 25-34,37,43-47,50-54,56-58,60,61,63-74 and 97-100* is/are rejected.

7)☒ Claim(s) *5,23,24,101 and 102* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/6/04; 9/30/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (Claim 1-12, 15-34, 37, 43-47, 50-54, 56-58, 60, 61, 63-74) in the reply filed on 2/22/07 is acknowledged. Newly added claims 97-102 are part of the elected invention of Group I.

The traversal is on the ground(s) that it would not impose an undue burden on the Examiner to search Group II with Group I as a search for one would overlap a search for the other. This is not found persuasive because of the following reasons. As regards search burden, the MPEP teaches "For purposes of the initial requirement, a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation of separate classification, or separate status in the art, or a different field of search as defined in MPEP § 808.02. That prima facie showing may be rebutted by appropriate showings or evidence by the applicant" (see MPEP 803). In the instant case, the inventions have been determined to have a separate classification and status in the art. As well, the different groups comprise divergent subject matter for which a search for art pertaining to each group is not coextensive. For example, a search for art for a regulated polymerase III expression system requires a search of the components of the product. However, in the event that the product is not patentable, a determination of whether each method of making and using the product is patentable over the art is based upon the particulars of the method and not on the product made by or used in the method. Conversely, a search of any given process of making or using the product does not adequately support patentability of the product because the product can be made by or used in a materially different process. Therefore, until the product is deemed allowable, search and

examination of the process claims with the product imposes an undue burden on the Office. As discussed previously, if a product claim is found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04..

The requirement is still deemed proper and is therefore made FINAL.

As well, applicants elect with traverse SEQ ID NO:1 in the response filed 2/22/07. Applicants argue that a total of two sequences is a reasonable number of sequences as applicants are not burdening the Office with dozens of additional sequences. Applicants' arguments have been considered but are not persuasive. Applicant is directed to the Pre-OG Notice published March 27 rescinding the 1996 OG Notice: Examination of Patent Applications. As set forth in this notice, the sequences will be examined for independence, relatedness, distinction and burden as for claims to any other type of molecule. MPEP 2434 is directed to examination of sequences and guidelines so established because of the enormous number of applications appearing in the office that comprise large numbers of nucleic acids. MPEP 2434 teaches, "Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141."

Claims 7, 75-77 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/22/07.

Drawings

Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Claim Objections

Claims 1, 31, 43, 44, 47, 60, 67 and 102 are objected to because of the following informalities: claims 1, 43 and 44 are objected to for recitation "first (second) element encoding". It is clear applicants intend by "element" that it is a nucleic acid that is encoding the transcription factor which is supported by a reading of the specification. However, use of the term "element" does not provide that kind of clarity and therefore it would be remedial to amend the claims to recite for example, --a first coding sequence encoding--.

Claim 31 is objected to as the word "by" has been inadvertently inserted following "RNA polymerase promoter" in line 2 .

Claim 47 recites "the selectable marker I" in claim 46. While there is antecedent basis for this limitation, the recitation that it depends from claim 46 appears to be an error as claim 46 recites that the gene is GFP. Hence it would need to be bother a selectable marker and GFP, and

these two types of genes are not so linked by the claim. Hence it would be remedial to amend the claim to depend from claim 44.

Claim 60 recites " a nucleic acid segment encoding a regulatory protein" which for clarity to distinguish to from the previously recited first and second nucleic acid segments, should be recited as --an additional nucleic acid segment encoding at least one regulatory protein--. Thus claim 61 will also provide adequate basis to recite in claim 62 --wherein the additional nucleic acid segment of claim 61 encodes--.

Claim 67 recites " a response element", however, it is proper to refer to previously recited limitations by using he article --the-- as opposed to "a".

Claim 102 recites " at least two nucleic acid segments", which for clarity to distinguish to from the previously recited first and second nucleic acid segments, should be recited as --at least two additional nucleic acid segments--. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 8 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The term "cells" defined by the specification at page 18, line 3-12 states that the cell is *in vitro* or *in vivo*. The scope of the claims, therefore encompasses a human being, which is non-statutory subject matter. As such, the recitation of the limitation "non-human" or "isolated" would be remedial. See 1077 O.G. 24, April 21, 1987.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 5, 22, 25, 30, 31, 34, 53, 54, 61 and 66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 25 and 30 recite the limitation "at least one binding site" in line 2. There is insufficient antecedent basis for this limitation in the claim. Claims 1 and 20 do not actually include a binding site operably linked to the recombinant polymerase IIII promoter.

Claim 5 is vague and indefinite in that the metes and bounds of "comprising the nucleic acid sequence as set forth in SEQ ID NO: 1" are unclear. It is unclear of the nucleic acid of claim 5 comprises in addition to the first and second segments f claim 1, the sequences of SEQ ID NO:1 or if the segments are encoded by SEQ ID NO: 1.

Claim 22 recite the limitation "the DNA binding domain" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 20 does not actually include a binding site operably linked to the recombinant polymerase IIII promoter.

Claim 34 recites the limitation "the polymerase III promoter element" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 53 and 54 are vague and indefinite in that the metes and bounds of "transgene comprises a hairpin RNA (ribozyme) are unclear. It is unclear if the transgene is intended to encode the hairpin RNA or ribozyme or if a hairpin RNA or ribozyme are in some other way associated with the sequence such as covalently attached to it.

Claim 61 is vague and indefinite in that the metes and bounds of "a regulatory protein which promoters transcription from the regulated promoter" are unclear. It is unclear what the relationship of the regulatory protein to the transcription factor is. It is unclear if the regulatory protein is in addition to the transcription factor or if the two are the same.

Claim 66 recites the limitation "a response element" in line 2. There is insufficient antecedent basis for this limitation in the claim. Claims 1 and 60 do not actually include a response element operably linked to the regulated promoter.

Claim Interpretation

The instant claims are drawn to a regulated polymerase III system comprising a recombinant polymerase III promoter that is regulated by a transcription factor whose expression is under control of an inducible promoter. During prosecution, claims must be interpreted as broadly as their terms reasonably allow. In the instant case, the term recombinant polymerase III promoter encompasses a variety of promoters whose relationship to pol III is not stated. Given the lack of structural requirements of the recombinant pol III, a broad interpretation of the claims *will include* an interpretation that the recombinant pol III promoter is any portion of the promoter in combination with any other promoter for example a TATA element. "While it is appropriate to use the specification to determine what applicant intends a term to mean, a positive limitation from the specification cannot be read into a claim that does not itself impose that limitation. A broad interpretation of a claim by USPTO personnel will reduce the possibility that the claim, when issued, will be interpreted more broadly than is justified or intended. An applicant can

always amend a claim during prosecution to better reflect the intended scope of the claim." MPEP 2105.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1, 2, 4, 8-12, 15-22, 25-33, 37, 43-45, 47, 50, 57, 58, 60, 61, 63-74, 97 and 99 are rejected under 35 U.S.C. 102(b) as being anticipated by Evans et al (US 2002/0177564; see entire document).

Evans et al teach an RNA polymerase III promoter. Given the lack of structural requirements of the recombinant pol III, a broad interpretation of the claims will include an interpretation that the recombinant pol III promoter is any portion of the promoter in combination with any other promoter for example a TATA element as demonstrated in figure 2. The recombinant promoter is operable linked to at least 4 ecdysone response elements. Transcription factors that bind to these response elements are encoded by nucleic acid segments that express the factors under inducible promoter (see e.g. ¶ 147) as recited in claims 1, 2, 4, 11, 19, 30, 31, 33, 37, 60 and 99. The transcription factors comprise RXR and VgEcR (which

alternatively can comprise a Gal4 domain) and are encoded by separate nucleic acid sequences and which encode DNA binding domains and transactivating domain (see e.g. figure 2). Expression by the transcription factor is dependent upon the presence of inducer (i.e. muristerone or ecdysone) as recited in claim 12, 20, 21, 29, 63-74 and 97. Expression of the transcription factors (also known as regulatory proteins) is under control of an inducible promoter such as a tissue specific promoter and other promoters that are developmentally, temporally or cell cycle regulated (see e.g. 0170) as well as promoters that are regulated by inducers as encompassed by claims 15-18 and 28 The vectors comprising these constructs are used in mammals, which encompass cells and non-human organisms (see e.g. ¶ 28 and 43) as recited in claims 8-10. The regulated promoter further expresses a second "element" such as a sequence of a transgene or an enzyme or reporter genes such as luciferase that emit light or fluoresce, transcription factors and cell surface receptors (see e.g. ¶ 27, 36, 41 and figure 3) as recited in claims 43-45, 50 and 100. The vector for expression is pBluescript, which comprises restriction sites downstream of the pol II promoter as recited in claim 57 and 58. As recited in claims 26, 27 and 32 muristerone does not affect binding affinity of RXR to the promoter (see e.g. figure 2).

Claim 1-4, 11, 25, 28, 29, 30, 31, 33, 34, 37, 43, 50-52, 56, 58, 60, 63-73, 98 and 99 are rejected under 35 U.S.C. 102(e) as being anticipated by Li et al (US 2004/0146858; see entire document).

Li et al teach an RNA polymerase III promoter (a mammalian U6 promoter) operably connected to a tetO site (see e.g. figure 3 and ¶ 120). Furthermore, a tet repressor is under expression of an inducible promoter (see e.g. ¶ 241-242) as recited in claims 1-4, 11, 25, 29, 30,

31, 33, 34, 37, 60, 63-73, 98 and 99. The vectors comprising these constructs are used therapeutically, which means that cells comprising the vector are found in the organisms that include as demonstrated in the examples, non human organisms as recited in claims 8-10. The recombinant pol III promoter is operably linked to siRNA as recited in claims 43, 50-52, 56. There are restriction sites downstream of the pol III promoter as illustrated in figure 1-2 and as recited in claim 58

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al (US 2002/0177564; see entire document) as applied to claim1, 2, 4, 8-12, 15-22, 25-33, 37, 43-45, 47, 50, 57, 58, 60, 61, 63-74, 97 and 99 above, and further in view of Cheng et al (Gene Therapy, 1997, Vol 4, 1013-1022; see entire document).

Applicants claim a regulated polymerase III expression system comprising a recombinant polymerase III promoter driving expression of a reporter such as GFP.

The teachings of Evans et al are described above and are applied as before except;

Evans et al do not teach use of GFP as a reporter.

Cheng et al teach use of GFP to assess gene transfer and expression in cells. Cheng et al teach that GFP is an important reporter molecule for non-invasively monitoring gene expression and protein localization with in cells, the fluorescence does not require other co-factors and improved GFP molecules have been made such as S65T and RSGFP4 (See bridging paragraph, page 1013-1032).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the reporter as taught by Evans et al with the GFP as taught by Cheng et al because Evans et al teach that it is within the ordinary skill of the art to express reporter genes from a recombinant promoter and because Cheng et al teach that it is within the ordinary skill of the art to use GFP as a reporter. One would have been motivated to do so in order to receive the expected benefit that GFP is an important reporter molecule for non-invasively monitoring gene expression and protein localization with in cells, the fluorescence does not require other co-factors and improved GFP molecules have been made such as S65T and RSGFP4. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

1-5,8-12,15-22, 25-34,37,43-47,50-54,56-58,60,61,63-74 and 97-100 are rejected.

Claim 6 is allowable as the art does not teach a nucleic acid comprising SEQ ID NO:1.

Claims 5, 23, 24, 101 and 102 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 102 is objected to for minor informalities.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maria B Marvich, PhD
Examiner
Art Unit 1633

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